STRUCTURAL BIOLOGY

Science for the 21st Century

will expand our knowledge of the shape of proteins and other macromolecules, its impact on biological function and its application to human health and other areas

Proteins contain coils, corkscrews, chains and side chains, threads and pleated sheets that twist, turn, loop, fold and refold into each other in elaborate, complicated 3-D structures. The distance between their components is measured in billionths of meters and they can act in milliseconds. A precise knowledge of their structural details is vital to understanding what they do, how they do it and what it means to living organisms.

Structural biology, in general, refers to research into the structure of proteins and other macromolecules, such as nucleic acids, and correlating information about these structures to biological function. At Los Alamos and elsewhere, the research is closely tied to work in several other fields, including the human genome, molecular medicine and bioengineering.

Proteins are the workhorses of biological life. They provide structure, control bodily functions, store and transport vital particles, help transmit neural impulses and bind to foreign objects as antibodies. Experimentalists obtain structural data about them with such techniques as X-ray and neutron crystallography, nuclear magnetic resonance, spectroscopy, and neutron and X-ray scattering, often in combination. Theorists model these data to predict the structure and function of other macromolecules, while seeking greater understanding of the physical principles of protein structure and dynamics to advance fundamental knowledge of biochemical processes.

Los Alamos — with its powerful computational capabilities, history of developing advanced biological techniques, large research facilities and multidisciplinary research environment — has made significant contributions to many techniques used to study structure. Laboratory researchers have designed novel software programs to present experimental results in useful ways and developed theories explaining the conformation of parts of proteins that are averse to water, a major influence on protein stability and dynamics.

A new protein crystallography experimental area at the Los Alamos Neutron Science Center will use neutrons to probe biological samples, producing “pictures” of proteins with the highest resolution currently possible when it becomes operational in 2000. Advances in neutron solution scattering techniques are helping Los Alamos researchers put single proteins together in larger groups, up to the level of complexity of viruses and ribosomes, to study how they assemble, interact and reassemble.

Los Alamos also is investigating structural genomics, a rapidly developing field whose goal is to identify and analyze the structures of all proteins in nature, including the approximately 60,000 in the human genome. In another area of research called kinetic crystallography, researchers trigger a protein reaction with light or radiation, then observe the resulting structural changes in close detail to obtain clues how it functions.

Future research in structural biology will proceed in two primary directions: developing a broader understanding of the nature and function of proteins and other macromolecules, and analyzing their specific activities in greater depth and detail. Greater knowledge of biological structure, combined with the results of research in related fields, will add to our basic understanding of biochemical processes. It also has practical benefits, most obviously in diagnosing and treating diseases. Other areas in which structural biology will play a major role include biotechnology, industrial processes, agriculture and environmental cleanup.

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